

the instant invention, 1, 23, and 26, require the analyte-binding partner to be present in the sorbent zone in excess relative to the analyte, so that “any analyte present in the defined volume is substantially depleted from the sample” (emphasis added). As explained on page 14, lines 17-22, of the instant specification, “substantially depleted” means that “at least about 60% of the analyte will be captured by a high affinity binding partner having a $K_A > 10^{10}$ liter mole⁻¹” (emphasis added).

As stated in the specification, page 7, lines 20 to 28, the assays of the present invention aim to maximize the signal the assay can generate. To achieve this goal, the microscopic sorbent zones used in the assays of the present invention are prepared to maximally perturb the sample concentration by harvesting the entire analyte mass onto the microscopic measurement region. In accordance with the assay regime of the present invention, the microscopic sorbent region acts as a sample concentration device, and the analyte mass present in an applied liquid volume, instead of analyte concentration, is detected.

Ekins *et al.*, on the other hand, teaches an assay that is totally different, to say the least, from the assay of the present invention. As discussed in the specification, page 2, lines 14 to 29, in the ambient analyte assay of Ekins *et al.*, the equilibrium number of analyte molecules bound by the solid phase is minimal relative to the number of analyte molecules present in the solution. Such a regime minimally perturbs the analyte concentration in the solution over the solid phase during the course of an assay. Therefore, assays of Ekins *et al.* are designed to measure the analyte concentration of a sample, instead of the analyte mass of the sample.

Specifically, the '202 patent is directed to the determination of ambient analyte concentrations in liquids. This assay requires minimal perturbation of the analyte concentration in the solution over the solid phase during the course of an assay. The '202 patent teaches that “only an

insignificant proportion of any analyte present in the liquid sample becomes bound to the binding agent” (claim 1, emphasis added). Similarly, the Immunoassay reference is also directed to an ambient analyte immunoassay. In the ambient analyte immunoassay, the proportion of bound analyte molecules is small and “the resulting reduction in the ambient analyte concentration may be ignored” (page 173, left column, emphasis added). This “ignored” amount of the analyte depleted from the sample is further defined as “less than 1%” by the reference (page 173, left column). Thus, the '202 patent and the Immunoassay reference, either alone or in combination, do not teach or suggest the analyte be substantially depleted from the sample. To the contrary, they teach away from the present invention by requiring that only an insignificant amount of the analyte (less than 1%) be depleted from the sample. In fact, if a substantial amount of analyte is depleted from the sample, as required by the present invention, the concentration of a sample would be maximally perturbed, and, therefore, resulting in an inaccurate measurement of the concentration of the sample in the assays of Ekins *et al.*

In light of the forgoing, applicants respectfully submit that the '202 patent and the Immunoassay reference, either alone or in combination, cannot make claims 1, 23, and 26 obvious. None of the cited references, either alone or in combination, would have motivated one skilled in the art to arrive at the present invention, which requires a substantial depletion of the analyte from a sample. Claims 2-4, 13-19, 24, and 25 depend, directly or indirectly, on claims 1, 23, and 26 and are not obvious for at least the same reasons. Accordingly, withdrawal of the rejection to claims 1-4, 13-19, and 23-26 is respectfully requested.

Claims 1-4, 13-19, 21, and 23-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent in view of Ekins *et al.*, Analytica Chimica Acta (Analytica reference). This rejection is respectfully traversed.

As discussed above, the '202 patent does not teach an assay that requires a substantial depletion of the analyte from a sample. The Analytica reference cannot remedy the defect of the '202 patent. As discussed in our previous response to the first Office Action, similarly to the Immunoassay reference, the Analytica reference discloses ambient analyte immunoassay. It is required by the method, that the proportion of bound analyte be so small that the "disturbance to the ambient analyte concentration can be ignored" (page 80, first paragraph). This "ignored" amount of the analyte depleted from the sample is further defined as "invariably less than 1% regardless of the analyte concentration" by the reference (page 80, first paragraph, last sentence). Therefore, like the Immunoassay reference, the Analytica reference does not teach or suggest the analyte being substantially depleted from the sample. Instead, the Analytica reference teaches away from the present invention by requiring that only an insignificant amount of the analyte (less than 1%) is depleted from the sample. In light of the foregoing, applicants respectfully submit that the '202 patent and the Analytica reference, either alone or in combination, cannot make claims 1, 23, and 26 obvious. Claims 2-4, 13-19, 24, and 25 depend, directly or indirectly, on claims 1, 23, and 26 and are not obvious for at least the same reasons. Accordingly, withdrawal of the rejection to claims 1-4, 13-19, 21, and 23-26 is respectfully requested.

Claims 5-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either the Immunoassay reference or the Analytica reference, in further view of Ullman *et al.* (U.S. Patent 5,512,659). Claim 11 is rejected under 35 U.S.C. § 103(a) as unpatentable over the '202 patent, and either the Immunoassay reference or the Analytica reference in further view of Waggoner *et al.* (U.S. Patent 5,368,486). Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either the Immunoassay reference or the Analytica reference in view of the Waggoner *et al.*, in further view of Lee *et al.* (U.S. Patent 5,453,505). Claim 20

is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either the Immunoassay reference or the Analytica reference in view of Northrup *et al.* (U.S. Patent 5,639,423). Applicants respectfully traverse these rejections.

As discussed above, the '202 patent, the Immunoassay reference, and the Analytica reference, either alone or in combination, cannot make claim 1 obvious, because they teach away from the binding assay of the present application, which requires the analyte to be substantially depleted from the sample. Claims 5-10, 11, 12, and 20 depend directly or indirectly from claim 1 and cannot be made obvious by the '202 patent, the Immunoassay reference, and the Analytica reference for at least the same reasons.

Ulman *et al.*, Waggoner *et al.*, Lee *et al.*, and Northrup *et al.* cannot remedy the defect of the '202 patent, the Immunoassay reference, and the Analytica reference, and are not relied upon by the Examiner for such. Ulman *et al.*, Waggoner *et al.*, Lee *et al.*, and Northrup *et al.* have no teaching whatsoever of a binding assay utilizing a plurality of sorbent zones containing an analyte binding partner, let alone a binding assay, which requires an excess of the analyte binding partner "relative to the analyte, so that any analyte present ... is substantially depleted from the sample." Therefore, none of the cited references, either alone or in combination, can motivate one skilled in the art to arrive at claims 5-10, 11, 12, and 20. Withdrawal of the rejection is, therefore, respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at Fullerton, California, telephone number 714/773-6929 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,

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